

# Changing Care Pathways and Between-Centre Practice Variations in Intensive Care for Traumatic Brain Injury across Europe – a CENTER-TBI analysis

Running title: Intensive care management after Traumatic Brain injury

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## Abstract

**Purpose:** To describe ICU stay, selected management aspects, and outcome of Intensive Care Unit (ICU) patients with traumatic brain injury (TBI) in Europe, and to quantify variation across centres.

**Methods:** Prospective observational multicentre study conducted across 18 countries in Europe and Israel. Admission characteristics, clinical data, and outcome were described at patient- and centre-level. Between-centre variation in the total ICU population was quantified with the median odds ratio (MOR), with correction for case-mix and random variation between centres.

**Results:** A total of 2138 patients were admitted to the ICU, with median age of 49 years; 36% of which were mild TBI (Glasgow Coma Scale; GCS 13-15). Within 72 hours 636 (30%) were discharged and 128 (6%) died. Early deaths and long stay patients (>72 hours) had more severe injuries based on the GCS and neuroimaging characteristics, compared with short stay patients. Long stay patients received more monitoring and were treated at higher intensity, and experienced worse 6-month outcome compared to short-stay patients. Between-centre variations were prominent in the proportion of short stay patients (MOR= 2.3,  $p<0.001$ ), use of Intracranial Pressure (ICP) monitoring (MOR= 2.5,  $p<0.001$ ) and aggressive treatments (MOR= 2.9,  $p<0.001$ ); and smaller in 6-month outcome (MOR= 1.2,  $p=0.01$ ).

**Conclusions:** Half of contemporary TBI patients at the ICU have mild to moderate head injury. Substantial between-centre variations exist in ICU stay and treatment policies, and less so in outcome. It remains unclear whether admission of short stay patients represents appropriate prudence or inappropriate use of clinical resources.

**Keywords:** intensive care unit, traumatic brain injury, intracranial pressure, outcome

**Take home message:** “Patients with traumatic brain injury admitted to intensive care units are older and often less severe than in previous studies. Substantial between-centre variation exists in ICU admission and treatment policies across Europe”

## Introduction

Traumatic brain injury (TBI) causes a social and economic global burden with about 82,000 deaths in Europe every year [1]. Patients with severe TBI often receive a highly intensive and multidisciplinary approach to prevent or mitigate both secondary brain injury and systemic complications [2]. For less severe TBI cases (without severe extracranial injury), clinicians have to estimate whether they will benefit from ICU admission, since guidelines with high-level evidence on ICU admission criteria are lacking. ICU admission is costly, and might also potentially be inappropriate for the patient, with risk of overtreatment and ICU-related complications, such as infections from multi-resistant bacteria [3].

In previous studies, intensive care admission was described merely for the most severe TBI cases, typically young male victims of high-energy road traffic incidents. In high income countries, however, the aging population and the reduction of road traffic incidents has led to important changes in TBI epidemiology, which now includes older patients, who are often victims of falls, and present with frequent co-morbidities but less severe brain injury. Recent data suggest that the landscape of TBI in Europe is changing and that, correspondingly, ICU admission policies may have been modified, including a larger proportion of milder TBI patients [4, 5].

The aims of this study were

- 1) to provide a general description of ICU stay, selected management aspects and outcome in TBI patients across Europe and
- 2) to quantify variation across centres.

## Methods

### *CENTER-TBI study*

The Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI study, registered at [clinicaltrials.gov](https://clinicaltrials.gov) NCT02210221) entails a longitudinal prospective collection of TBI patient data across 63 centers in Europe and Israel between December 19, 2014 and December 17, 2017. Inclusion criteria were: (1) clinical diagnosis of TBI; (2) indication for a brain CT scan; and (3) presentation to the hospital within 24 hours post-injury. The presence of a severe preexisting neurological disorder, potentially confounding outcome assessment, was the only exclusion criterion. The CENTER-TBI study was approved by the medical ethics committees of all participating centres and informed consent from the patient or legal representative was obtained according to local regulations [4, 6].

### *ICU population and data collection*

All patients directly admitted from the Emergency Room or transferred within 24 hours of injury from another hospital to the ICU were analyzed [4]. Patients who deteriorated at the trauma, neurological or neurosurgical ward and were (re)admitted to the ICU were not included. Clinical data were collected at ICU admission, during ICU stay and at ICU discharge. For the current study, we extracted data on demographics, injury, imaging, admission, monitoring, treatment, and outcome characteristics. Patients were stratified using baseline GCS scores as mild (GCS 13-15), moderate (GCS 9-12), or severe TBI (GCS <9) [4].

### *ICP and ICP-lowering treatments*

ICP and cerebral perfusion pressure (CPP) values were collected every two hours. Intracranial hypertension was defined as a value above 20 mmHg, while 60 mmHg was chosen as a threshold for low CPP. To quantify the intensity of ICP-targeted therapies, a recently updated and validated version of the therapy intensity level (TIL) scale was used [7]. This scale summarizes in a score the number and the intensity of treatments. In addition, we analyzed the use of aggressive treatments for raised ICP as hypothermia, intense hypocapnia, barbiturates and decompressive craniectomy.

### *Outcome*

Outcome was measured at six months after injury using the Glasgow Outcome Scale – Extended (GOSE), administered by interview or postal questionnaire. The categories ‘vegetative state (GOSE 2)’ and ‘lower severe disability (GOSE 3)’ were combined, resulting in a seven-point ordinal scale.

### *Statistical analysis*

Patient characteristics are described as mean and standard deviation (SD) or as median and interquartile range [IQR]. We defined three groups: early deaths (died within  $\leq 72$  hours of ICU admission), short stay ( $\leq 72$  hours in the ICU) and long stay ( $> 72$  hours in the ICU). Patient characteristics, treatments and outcome were compared between these groups with  $\chi^2$  - tests for categorical variables and ANOVA and t-tests for continuous variables. We used the IMPACT Core model to calculate expected mortality and proportion with unfavourable outcome (GOSE < 5).

The variation between centres was quantified using random effect logistic and ordinal regression models with a random intercept for centre, and expressed as the Median Odds Ratio [8] for:

- 1) The proportion of patients with a short stay ( $\leq 72$  hours in the ICU) versus long stay ( $> 72$  hours) and early deaths ( $\leq 72$  hours).
- 2) The proportion of cases having received ICP monitoring. Also, a sensitivity analysis of the proportion of cases having received ICP monitoring in a subset of patients with a GCS  $\leq 8$  and CT abnormalities was performed.

- 3) The use of aggressive ICP-lowering treatments (any use of Decompressive Craniectomy, Metabolic Suppression, Hypothermia Therapy or Intensive Hypocapnia)
- 4) 6-months GOSE outcome

The MOR is a measure of variation in treatments or outcomes between hospitals that is not explained by factors in the model or attributable to chance. The MOR is related to  $\tau^2$ , which is the variance of the random effects;

$$MOR = exp[\sqrt{2 \times \tau^2 \times 0.6745}] \approx exp(0.95\tau)$$

The MOR can be interpreted as the odds ratio for comparing two randomly selected centres. For example, a MOR equal to one, indicates no differences between centres. If there is considerable between-centre variation, the MOR will be large. For example a MOR of 2 for a certain treatment, indicates that if two TBI patients with the same injury severity and characteristics presented to two random centres in our sample, one patient will have an over twofold probability to receive that treatment. To adjust for differences in baseline risk, we included the variables from the International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT) lab prognostic model [9] and any major extracranial Injury (defined as an Abbreviated Injury Scale (AIS) > 3) [10]. The Likelihood ratio test was used to determine the significance of the between-center variation, comparing a model with and without a random effect for center. The corresponding p-values require a mixture distribution since the null hypothesis is on the boundary of the parameter space) [11].

Statistical analyses were performed in the R statistical software [12]. Multiple imputation was used to handle missing values, with use of the mice package in R [13]. These analyses were based on Version 2.0 of the CENTER-TBI core dataset, accessed using a bespoke data management tool, ‘Neurobot’ (<http://neurobot.incf.org>; RRID: SCR\_01700).

## Results

### *Patient characteristics*

A total of 4509 patients were enrolled in the CENTER-TBI study, 2138 of whom were admitted to the ICU and included in this study. Patients were mostly male (73%). The median age was 49 years (IQR 29-65). A minority were children younger than 18 years (132, 6%), 552 (26%) were older than 65 years and 94 (4%) older than 80 years. Patients with severe TBI constituted (48%) of the ICU admissions, while 720 cases (36%) were classified as mild. Major extra-cranial injuries were present in 1174 (55%) patients. (Table 1) More than half of the 54 ICUs have a neuro-ICU available (35, 65%). The median number of ICU beds available was 35 [28-45]. Thirty-eight ICUs had a step-down-unit available (70%). (Table S1) The median number of ICU patients recruited was 28 with an IQR of 15-50 (range 1-140). The median length of stay for the entire ICU cohort was 11 (IQR 3- 26) days.

ICU mortality and discharge rates were high in the first 72 hours, but declined over time (Figure 1, Figure 2). There were 128 (6%) early deaths, 636 (30%) short stay, and 1372 (64%) long stay cases (Figure 2).

Early death patients had a higher median age (62 years) and more severe injuries, both intracranial and extra-cranial, compared to survivors. Demographic features were comparable between short stay and long stay groups, while significant differences were identified with respect to injury severity, CT findings, and pre-admission insults. (Table 1) The main cause of mortality in early death patients was due to initial head injury (78, 81%). (Figure S2)

The most frequent reason for admission in short stay patients were need for frequent neurological observations (340; 54%) and mechanical ventilation (154; 24%) (Figure S3). The long stay patients included 319 patients (25%) classified as mild TBI in whom similar reasons for admission were mentioned (the need for neurological observations (152, 48%), mechanical ventilation (96, 30%).

### *Monitoring and treatment*

Mechanical ventilation for at least 24 hours was most often applied in long stay patients and in patients who died early, when compared to short stay patients (1164 [85%] and 91 [71%]; versus 201 [32%], respectively). A large difference was found in the use of ICP monitoring between long stay and short stay cases (837; 62% versus: 41; 7%, respectively). The main indication for ICP monitoring in short stay patients was surveillance after intracranial operation (31, 76%). Invasive blood pressure monitoring was used in the majority of long stay patients (1227; 90%) and in early deaths (113; 89%); but less frequently (388; 62%) in short stay patients. (Table S2)

Both neurosurgical interventions and extracranial surgery were more common in long stay patients (634; 47% and 467; 34%, respectively) when compared to short stay patients (139; 22% and 122; 19%, respectively). Patients in the short stay group rarely ( $\leq 5\%$ ) received aggressive ICP treatments (i.e. decompressive craniectomy, metabolic suppression, hypothermia, or intensive hypocapnia). (Table S2)

### *Complications and Outcome*

Long stay patients suffered more complications compared with short stay patients: most commonly ventilator acquired pneumonia (276; 21% versus 3; 0.5%) and cardiovascular complications (125; 9.3% versus 9; 1.5). The overall median hospital length of stay was 11 days (IQR: 3.4-26), while the median hospital length of stay for long stay patients was 18 days (IQR: 7.7-35). When compared to long stay patients, short stay patients were less often discharged to a step down unit (86 [14%] vs 255 [21%] respectively), and more often transferred to the ward (486 [78%] versus 616 [51%]). Long stay patients were also often discharged to other hospitals (174; 14%) and rehabilitation units (95; 8%), while other discharge locations (such as home, other ICU, or nursing home) were rare. (Table 2)

In-hospital mortality for the ICU stratum was 15%; and at six months mortality rose to 21% (data available for 1846 cases), which was lower than expected mortality based on the IMPACT model (30%). Six-month mortality was higher in the long stay patient group compared with the short stay group (20% versus 5.5%).(Table 2)

An unfavorable outcome at six months (GOSE  $< 5$ ) was observed in 43% in the total ICU stratum, 50% (590) in long stay group, and in 15% in short stay group (77). The unfavourable outcome rate in the total ICU stratum was similar to the expected rate based on the IMPACT model (49%)

### *Between centre- differences*

Substantial between-centre differences were found in the proportion of short stay, long stay and early deaths (MOR: 2.3,  $p < 0.001$ , Figure 4). When adjusted for case-mix and random variation, between-centre variation in the proportions of patients in the short stay versus long stay and early death groups was still substantial (MOR: 2.3,  $p < 0.001$ ).

Regarding ICP monitoring, after adjustment for case-mix, substantial and significant between-centre variation persisted in the use of ICP monitoring (MOR: 2.5,  $p < 0.001$ , Figure 4). A sensitivity analyses (with a subset of patient with a GCS  $\leq 8$  and CT abnormalities) confirmed this between-centre variation (MOR: 2.6,  $p < 0.001$ ). After case-mix adjustment, significant between-centre differences were also found in the use of aggressive therapies (MOR: 2.9,  $p < 0.001$ , Figure 4).

Between-centre variation in outcome was smaller compared to the variation in treatment. The MOR in the total ICU population for six month GOSE was 1.2 ( $p = 0.01$ , Figure 4).

## Discussion

The aims of this study were to describe ICU admission policies, selected management aspects, and outcome in TBI patients across Europe both at the patient and centre level. A substantial proportion of patients admitted to the ICU were classified on presentation as having a mild or moderate TBI. This is in strong contrast with historical TBI series, such as the USA Traumatic Coma Data Bank study [14] and other studies [15]. However, those series included only severe TBI patients, so that any evaluation of the general ICU admission policies at that time for milder cases is impossible. A more recent study, which analyzed data from 1648 mild TBI patients in 11 US level I trauma centres, showed that about 24 percent of them required admission to the ICU at some stage [16].

Even when compared to these latter data, our findings indicate quite liberal ICU admission rates for less severe cases. This is consistent with the strategies declared by the majority of centres participating in CENTER TBI. When centres were asked (in the Provider Profiling survey; see [5]) if they would admit "patients with a Glasgow Coma Score (GCS) between 13 and 15 without CT abnormalities but with other risk factors", 68% of responders reported this as consistent with their centre policy.

Among the cases admitted, we looked at three different patient groups. Around 6% of patients died in the first 3 days after admission, with clearly severe intracranial and extra-cranial injuries. Patients in this group were significantly older, and only approximately half of those with documented intracranial mass lesions in this group received an operation. In survivors, we studied two distinct groups; those with a brief transition through the ICU and the second characterized by a prolonged ICU treatment. We selected the first 72 hours as criterion to separate these two patient streams, triggered by the high ICU discharge rate during the first 3 days. This separation identified patients with different clinical characteristics, care pathways, and outcomes: long stay patients were more severely injured, required more frequent invasive monitoring (including ICP) and therapies (both surgical and medical), and suffered a worse outcome. In contrast, short stay patients were less severely injured, received less monitoring and treatments, and achieved better outcomes. The most frequently indicated reasons for ICU admission in this latter group were the need for strict neurological observation and mechanical ventilation (which, however, was continued for at least 24 hours only in a third of cases). This may reflect current policy of early intubation at the scene of accident, and/or during initial assessment and evaluation. Cranial and extra-cranial surgery could also have been alternative indications for a short period of intense post-operative observation in the ICU.

These data can be interpreted in one of two ways. On one hand, the observed practice may represent a prudent strategy, offering close surveillance and assistance to patients at relatively low risk, but with the opportunity to ensure consistently good outcomes. The risk of deterioration in mild TBI is low but non-negligible. A recent meta-analysis, including 45 studies (for a total of 65724 patients), estimated a 12% incidence of neurological deterioration and 3.5% neurosurgical intervention in mild TBI (characterized as GCS 13-15) [17]. Alternatively, the observed admission strategies may represent costly over-triage, because the ICU is an expensive resource, which should be used wisely. The fact that 11 patients in the short stay group were discharged home directly from the ICU raises strong reservations on their need for intensive care. A previous study in mild TBI patients in the ICU in the USA showed that 17% of cases were over-triaged, with over triaged patients defined as "*ICU stay  $\leq$  1 day; hospital stay  $\leq$  2 days; no intubation; no neurosurgery; and discharged to home*"[18]. Our data on ICU admission of mild TBI patients are partially concordant with these findings, and while they do not permit accurate cost-benefit analysis, they clearly indicate a trend in ICU admission policies that deserves attention.

After adjustment for case-mix and random variation between centres, we found significant between-centre proportion of short stay patients discharged alive within 72 hours. This confirms the results of earlier studies that found large variation in admission and discharge policies, primarily for mild TBI patients [5, 18]. This variation might reflect various factors: a search towards more individualized management [2], a lower adherence to guidelines [19], different availability of resources, or various combinations of these different factors. As for monitoring and management variations among centres,



heterogeneity was not unexpected: previous studies [19-21] and surveys [22-24] found profound dissimilarities between centres in monitoring and treatment policies similar to our study.

The MOR for outcome between centres (1.2) was significant ( $p = 0.01$ ), but smaller than the MOR for case-mix, ICP monitoring and aggressive therapies (2.5 - 2.9). This may reflect the small proportion of outcome variance modifiable by differences in management, and/or that differences in individual aspects of management may be discordant and make any outcome impact less easily detectable. Further, between-centre variations in outcome that we demonstrated were smaller than previously reported [25, 26]. This may be because previous analyses were based on older data, collected across multiple studies, and heterogeneity in time and location explained the larger outcome variance in these older reports. It is also possible that over time, a more homogeneous standard of treatment has evolved in Europe and Israel.

### *Strengths and Limitations*

The CENTER-TBI study is unique for its extensive data collection in multiple centres, enrolling TBI patients with varying injury severity across a wide range of European centres. Limitations include that we focused on the ICU while an individual patient's fate, and policies of the center at which treatment is delivered, depend on the continuum of care (from pre-hospital to rehabilitation). Second, the centres differed in their ICU characteristics, which might potentially contribute to between-centre differences in ICU stay, treatment and outcome. In addition, we might have missed some important case-mix variables in the models that might have contributed to differences between centres (instead of true differences in policies). Third, the low number and non-consecutive enrolment in some centres could result in non-representative recruitment with reference to local ICU admission policy and introduce selection bias. Finally, all centres participating in CENTER TBI are characterized by their commitment to TBI research. They might represent a selected sample of the neuro-trauma centres in Europe limiting generalizability.

### *Future directions*

The observed between-centre differences in ICU policies require further research on whether these differences impact patient outcome. Comparative Effectiveness Research (CER) can be used for this purpose [27], requiring adequate covariate adjustment to account for confounders, and adjustment for other treatment policies that might differ between the centers. Variation in ICU performance also provides opportunities for future benchmarking and quality initiatives.

### **Conclusions**

Our results confirm that the current ICU patient population admitted with Traumatic Brain Injury across Europe has changed, compared to previous data, and now includes older patients and a substantial proportion of mild and moderate cases. Sub-populations of patients (which we defined as short stay, long stay, and early mortality groups), are clearly different in injury severities, indications for ICU admission, care pathways, ICU resource utilization, and outcome. Our per-centre analysis identified differences in the proportion of short stay patients and interventions, for instance in the use of ICP monitoring and aggressive therapy, while there were only small differences in outcome.

## List of abbreviations

AIS: Abbreviated injury scale; CENTER-TBI: Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; CPP: Cerebral perfusion pressure; CT: Computer tomography; EDH: Epidural hematoma;; GCS: Glasgow Coma Scale; GOSE: Glasgow Outcome Scale Extended; ICP: Intracranial pressure; ICU: intensive care unit; IMPACT: International Mission for Prognosis and Analysis of Clinical Trials; MOR: Median odds ratio; tSAH: Traumatic Subarachnoid Hemorrhage; TBI: Traumatic brain injury; US: United States

## Declarations

### *Ethics approval and consent to participate*

In each recruiting site ethical approval was given; an overview is available online [28]

### *Consent for publication*

Not applicable

### *Availability of data and materials*

The datasets used and/or analyzed during the current study are available via <https://www.center-tbi.eu/data> on reasonable request.

### *Competing interests*

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### *Authors' contributions*

JH and EW analyzed the data and drafted the tables and figures. JH, EW, and NS interpreted the data and drafted the manuscript. NS designed the study protocol and supervised the study. HL, GC, AM, and DM were involved in regular meetings on the manuscript and reviewed the manuscript multiple times. All authors were involved in the design of the CENTER-TBI study and reviewed and approved the final version of the manuscript.

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Table 1: Baseline characteristics

	<b>Total</b>	<b>Short stay</b>	<b>Long stay</b>	<b>Early deaths</b>	<b>P-value</b>
	<b>2138</b>	<b>636</b>	<b>1372</b>	<b>128</b>	
Age (median (IQR))	49 (29 – 65)	48 (28 – 64)	49 (29 – 64)	62 (40 – 75)	<0.001
>=65 years	552/2138 (26%)	153/636 (24%)	337/1372 (25%)	62/128 (48%)	<0.001
>=80 years	94 /2138(4.4%)	29/636 (4.6%)	52/1372 (3.8%)	13/128 (10%)	0.003
Male sex	1562/2138 (73%)	443/636 (70%)	1023/1372 (75%)	94/128 (73%)	0.07
Severity TBI					<0.001
Mild	720/2009 (36%)	394/607 (65%)	319/1285 (25%)	6/116 (5.2%)	
Moderate	328/2009 (16%)	107/607 (18%)	213/1285 (17%)	8/116 (6.9%)	
Severe	961/2009 (48%)	106/607 (18%)	753/1285 (59%)	102/116 (88%)	
Pupillary Reactivity					<0.001
Both Reacting	1636/2016 (81%)	564/606 (93%)	1040/1287 (81%)	31/122 (25%)	
Both	246/2016 (12%)	16/606 (2.6%)	150/1287 (12%)	80/122 (65%)	
Unreacting					
One reacting	134/2016 (6.6%)	26/606 (4.3%)	97/1287 (7.5%)	11/122 (9.0%)	
Hypoxia	266/1981 (13%)	38/593 (6.4%)	191/1266 (15%)	37/121 (31%)	<0.001
Hypotension	267/1992 (13%)	36/595 (6.1%)	189/1274 (15%)	42/122 (34%)	<0.001
ISS (median (IQR))	29 (25 – 41)	24 (16 – 29)	34 (25 – 43)	58 (28 – 75)	<0.001
Any major extracranial injury (AIS>=3)	1174/2138 (55%)	283/636 (45%)	823/1372 (60%)	67/128 (53%)	<0.001
<i>CT Characteristics</i>					
Marshall CT Classification					<0.001
I	204/1854 (11%)	110/566 (19%)	90/1179 (7.6%)	3/108 (2.8%)	
II	889/1854 (48%)	330/566 (58%)	553/1179 (47%)	6/108 (5.6%)	
III	152/1854 (8.2%)	19/566 (3.4%)	105/1179 (8.9%)	28/108 (26%)	
IV	28/1854 (1.5%)	4/566 (0.7%)	17/1179 (1.4%)	7/108 (6.5%)	
V/VI	581/1854 (31%)	103/566 (18%)	414/1179 (35%)	64/108 (59%)	
Epidural Hematoma	369/1854 (20%)	120/566 (21%)	234/1179 (20%)	15/108 (14%)	0.22
tSAH	1347/1854 (73%)	318/566 (56%)	930/1179 (79%)	99/108 (92%)	<0.001
Contusion	1032/1854 (56%)	244/566 (43%)	730/1179 (62%)	58/108 (54%)	<0.001
Acute Subdural Hematoma	911/1854 (49%)	192/566 (34%)	633/1179 (54%)	86/108 (80%)	<0.001
Midline Shift	404/1854 (22%)	77/566 (14%)	281/1179 (24%)	54/108 (50%)	<0.001
Basal Cistern	586/1854 (32%)	81/566 (14%)	415/1179 (35%)	94/108 (87%)	<0.001
Absent or Compressed					

This table shows the baseline characteristics for short stay (stay  $\leq 72$  hours), Long Stay (stay  $>72$  hours), and early deaths ( $\leq 72$  hours). P-values from ANOVA and chi-square statistics for continuous and categorical characteristics respectively

AIS: Abbreviated Injury Scale. tSAH: traumatic subarachnoid hemorrhage

Table 2: Outcome and Complications

	<b>Total</b>	<b>Short stay</b>	<b>Long Stay</b>	<b>p-value</b>
	<b>2138</b>	<b>636</b>	<b>1372</b>	
<i>Outcomes</i>				
6-month Mortality	394/1846 (21%)	29/531 (5.5%)	237/1187 (20%)	<0.001
6-month Unfavorable Outcome (GOSE<5)	795/1846 (43%)	77/531 (15%)	590/1187 (50%)	<0.001
Hospital Length of stay in days (median (IQR))	11 (3.4 – 26)	6.3 (3.0– 11)	18 (7.7 – 35)	<0.001
Discharge Location from ICU				<0.001
General Ward	1102/1840 (60%)	486/623 (78%)	616/1216 (51%)	
Home	15/1840 (0.8%)	11/623 (1.8%)	4/1216 (0.3%)	
Nursing Home	4/1840 (0.2%)	2/623 (0.3%)	2/1216 (0.2%)	
Other	36/1840 (2.0%)	5/623 (0.8%)	30/1216 (2.4%)	
Other Hospital	201/1840 (11%)	27/623 (4.3%)	174/1216 (14%)	
Other ICU	43/1840 (2.3%)	3/623 (0.5%)	40/1216 (3.3%)	
Rehab Unit	98/1840 (5.3%)	3/623 (0.5%)	95/1216 (7.8%)	
Step down/ High Care Unit	341/1840 (19%)	86/623 (13.8%)	255/1216 (21%)	
<i>Complications at the ICU</i>				
Ventilator Acquired Pneumonia	280/2090 (13%)	3/616 (0.5%)	276/1347 (21%)	<0.001
Cardiovascular Complications	155/2091 (7.4%)	9/616 (1.5%)	125/1348 (9.3%)	<0.001
Meningitis	49/2090 (2.3%)	0/616 (0.0%)	48/1347 (3.6%)	<0.001
Seizures	121/2089 (5.8%)	17/616 (2.8%)	99/1346 (7.4%)	<0.001

This table shows the outcomes and ICU complications for patients surviving more than 72 hours after ICU admission. The data is shown for short stay (stay  $\leq$  72 hours) or long stay (stay  $>$ 72 hours) patients. Early deaths are not included in this table as these patients represent the outcome in itself (death) and follow-up cannot be described. The categories 'vegetative state (GOSE 2)' and 'lower severe disability (GOSE 3)' were combined resulting in a seven-point ordinal scale.'

GOSE: Glasgow Outcome Scale Extended, ICU: Intensive Care Unit, IQR: interquartile range. P-values from ANOVA and chi-square statistics for continuous and categorical characteristics respectively

## Figures in article

### Figure 1: ICU patient flow over time

Legend 1A] Plot of the dynamic states of patients with TBI that were admitted to the ICU during the first seven days after ICU admission. The y-axis represents the probability to be in one of the possible states (i.e. alive or dead or discharged from ICU) at each time point from ICU admission. \*Died after ICU discharge.

Legend 1 B] Plot of the dynamic states of patients with TBI that were admitted to the ICU during the first six months after ICU admission. The y-axis represents the probability the be in one of the possible states (i.e. alive or dead or discharged from ICU) at each point from ICU admission. \*Still in ICU

### Figure 2: Flowchart of ICU patients

This figure shows the flow of patients at the ICU, based on their length of stay. \*Patients that died within 72 hours at the ICU

### Figure 3: Six-month Glasgow Outcome Scale Extended

Legend Figure 2: This figure shows the distribution of the functional outcomes at the GOSE after 6 months for all ICU patients, short stay patients, and Long Stay patients.

### Figure 4: Between-centre differences in ICU policies and outcome

Legend Figure 3: This panel shows the adjusted differences (adjusted for case-mix with the IMPACT prognostic model) between centres by considering [A] The proportion of patients with a short stay ( $\leq 72$  hours in the ICU) versus long stay ( $> 72$  hours) and early deaths ( $\leq 72$  hours); long stay and early deaths were treated as one group, since they resemble more severe patients and we aimed to study the proportion in each centre of short stay patients that were discharged alive within 72 hours. [B] GOSE at 6 months for total ICU population, [C] ICP monitoring, [D] Aggressive Therapy (any use of Decompressive Craniectomy, Metabolic Suppression, Hypothermia Therapy or Intensive Hypocapnia during ICU stay). A random effect regression model was used to correct for random variation and adjusted for case-mix severity using the IMPACT variables and the presence of any major extracranial injury. The MOR reflects the between-centre variation; a MOR equal to 1 represents no variation, the larger the MOR, the larger the variation. Significant differences (  $p$ -value  $< 0.001$ ) are present for data shown in panels [A], [C], and [D] for panel B ( $p=0.01$ )

GOSE: Glasgow Outcome Scale extended, ICP: intracranial pressure, MOR: median odds ratio











